



Appl. Serial No. 09/624,530

Amended dated August 4, 2005

Response to Office Action dated May 4, 2005

II. AMENDMENT OF CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application.

LISTING OF CLAIMS

Claims 1-5.(Cancelled)

Claim 6.(Currently Amended) A method for treating pain in humans for a time period of ~~about~~ 24 hours, comprising administering to a human patient at a dosing interval of about 24 hours, a solid, controlled-release oral dosage form comprising an analgesically effective amount of ~~an opioid analgesic~~ hydromorphone or a pharmaceutically acceptable salt thereof or a mixture of opioid analgesics or a salt thereof, incorporated into a controlled-release matrix, wherein the dissolution rate in vitro of the dosage form, when measured by the USP Paddle Method of U.S. Pharmacopeia XXII (1990) at 100 rpm at 900 ml aqueous buffer at pH 1.6 and 7.2 and at 37°C is from ~~about~~ 12.5% to ~~about~~ 42.5% (by wt) ~~opioid~~ hydromorphone or pharmaceutically acceptable salt thereof released after 1 hour, from ~~about~~ 25% to ~~about~~ 65% (by wt) ~~opioid~~ hydromorphone or pharmaceutically acceptable salt thereof released after 2 hours, from ~~about~~ 45% to ~~about~~ 85% (by wt) ~~opioid~~ hydromorphone or pharmaceutically acceptable salt thereof released after 4 hours and greater than 60% (by wt) ~~opioid~~ hydromorphone or pharmaceutically acceptable salt thereof released after 8 hours, the in-vitro release rate being substantially independent of pH in that a difference, at any given time, between an amount of ~~opioid~~ hydromorphone or pharmaceutically acceptable salt thereof released at one pH and an amount released at any other pH, when measured in-vitro using the USP Paddle Method of U.S. Pharmacopeia XXII (1990) at 100 rpm in 900 ml aqueous buffer is no greater than 10%, the dosage form further providing a the in-vitro release rate being chosen such that the peak plasma level of hydromorphone said opioid obtained in-vivo which occurs between at least 4 and to about 8 hours after administration of the dosage form, said dosage form providing a duration of therapeutic effect of about at least 24 hours and providing mean blood levels of hydromorphone

over 500 pg/ml at 12 hours after administration to human patients, and over 300 pg/ml at 24 hours after administration to human patients.

Claim 7. (Currently Amended) The method of claim 6, wherein said ~~opioid~~ analgesic is selected from the group consisting of hydromorphone, oxycodone, morphine, levorphanol, methadone, meperidine, heroin, dihydrocodeine, codeine, dihydromorphine, buprenorphine, salts thereof, and mixtures thereof dosage form comprises a pharmaceutically acceptable salt of hydromorphone.

Claim 8. (Currently Amended) The method of claim 6, wherein said dosage form ~~opioid~~ analgesic comprises hydromorphone hydrochloride.

Claims 9-12. (Cancelled)

Claim 13. (Previously Presented) The method of claim 6, wherein the controlled release matrix comprises a polymer selected from the group consisting of a pharmaceutically acceptable gum, an alkylcellulose, a cellulose ether, an acrylic resin, and mixtures of the foregoing.

Claim 14. (Previously Presented) The method of claim 13, wherein the matrix further comprises a digestible substituted or unsubstituted C₈-C₅₀ hydrocarbon.

Claim 15. (Previously Presented) The method of claim 14, wherein said hydrocarbon is selected from the group consisting of fatty acids, fatty alcohols, mineral oils, vegetable oils, waxes and mixtures of any of the foregoing.

Claim 16. (Previously Presented) The method of claim 13, wherein said dosage form further comprises a polyalkyleneglycol.

Claims 17-20. (Cancelled)

Claim 21. (Currently Amended) The method of claim 6, wherein said ~~opioid~~ dosage form comprises ~~consists of~~ from about 4 mg to about 64 mg hydromorphone.

Claim 22-23. (Cancelled)

Claim 24. (Currently Amended) A method for treating pain in humans for a time period of about 24 hours, comprising administering to a human patient at a dosing interval of about 24 hours, a solid, controlled-release oral dosage form consisting essentially of an analgesically effective amount of ~~an opioid analgesic~~ hydromorphone or a pharmaceutically acceptable salt thereof ~~or a mixture of opioid analgesics or a salt thereof~~, incorporated into a controlled-release matrix, wherein the dissolution rate in vitro of the dosage form, when measured by the USP Paddle Method of U.S. Pharmacopeia XXII (1990) at 100 rpm at 900 ml aqueous buffer at pH 1.6 and 7.2 and at 37°C is from about 12.5% to about 42.5% (by wt) ~~opioid~~ hydromorphone or pharmaceutically acceptable salt thereof released after 1 hour, from about 25% to about 65% (by wt) ~~opioid~~ hydromorphone or pharmaceutically acceptable salt thereof released after 2 hours, from about 45% to about 85% (by wt) ~~opioid~~ hydromorphone or pharmaceutically acceptable salt thereof released after 4 hours and greater than 60% (by wt) ~~opioid~~ hydromorphone or pharmaceutically acceptable salt thereof released after 8 hours, the in-vitro release rate being substantially independent of pH in that a difference, at any given time, between an amount of ~~opioid hydromorphone hydrochloride or a pharmaceutically acceptable salt thereof~~ released at one pH and an amount released at any other pH, when measured in-vitro using the USP Paddle Method of U.S. Pharmacopeia XXII (1990) at 100 rpm in 900 ml aqueous buffer is no greater than 10%, the dosage form further providing a the in-vitro release rate being chosen such that the peak plasma level of said ~~opioid~~ hydromorphone obtained in-vivo which occurs between at least 4 to about 8 hours after administration of the dosage form, said dosage form providing a duration of therapeutic effect of about at least 24 hours and providing mean blood levels of hydromorphone over 500 pg/ml at 12 hours after administration to human patients, and at least 300 pg/ml at 24 hours after administration to human patients.